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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,443	02/22/2006	Volety Srinivas	595222000100	4273

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EXAMINER	
TSAY, MARSHA M	

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1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/528,443	SRINIVAS ET AL.	
	Examiner	Art Unit	
	Marsha M. Tsay	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-11 and 13-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-11 and 13-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

This Office action is in response to Applicants' remarks received May 7, 2007. Claims 2, 12 are canceled. Claims 1, 3-11, 13-20 are pending and currently under examination.

Applicants' arguments have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous Office actions are hereby withdrawn.

Priority: The priority date is December 30, 2003.

Objections and Rejections

As stated in the prior Office action, many claims are replete with grammatical errors and should be corrected accordingly.

Claims 7-8 are objected to because of the following informalities: in claims 7-8, there should be a "the" inserted between "in presence". Appropriate correction is required.

35 U.S.C. 112, first paragraph, requires the specification to be written in "full, clear, concise, and exact terms." The specification is replete with terms which are not clear, concise and exact. The specification should be revised carefully in order to comply with 35 U.S.C. 112, first paragraph. Examples of some unclear, inexact or verbose terms used in the specification are: on page 3, line3, the term "Argnine Hydrochloride" should be corrected to "Arginine Hydrochloride" and there should also be a period at the end of the sentence; on page 3, line 15, the term "Argnine Hydrochloride" should be corrected to "Arginine Hydrochloride; on page 3 line 20, the term "Arginin hydrochloride" should be corrected to "Arginine Hydrochloride"; on

page 3 line 23, the term "Arg,HCl" should be corrected to "Arg.HCl". This is not an exhaustive list of all the grammatical errors present in the specification. Applicants are asked to carefully review and revise the specification accordingly.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-11, 13-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for enhancing molecular chaperone activity of wildtype α-crystallin with Arg.HCl and mutations in αA- and αB-crystallin at residues 116 and 120, respectively (αA-crystallin mutant R116C and αB-crystallin mutant R120G) with Arg.HCl, does not reasonably provide enablement for enhancing molecular chaperone activity of active mutants of αA-crystallin with Arg.HCl. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The scope of the instant claims is not commensurate with the enablement of the instant disclosure, because practice of the claimed invention would require undue experimentation by an artisan of ordinary skill in the art to ascertain which mutants of α-crystallin function in the same way as the wild-type protein. Thus there could be thousands of variants which contain substitutions, deletions, additions etc. Thus for the instant claimed invention, it would require an undue burden of experimentation for a skilled artisan to determine exactly which derivatives or fragments were active.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

In the instant case the quantity of experimentation would be large since there are myriad substitutions, deletions or insertions to choose from. The amount of guidance in the specification is minimal with regard to which amino acids in α-crystallin are essential for activity. Minimal examples are present of mutant α-crystallin proteins, only one specific example is provided each for αA- and αB-crystallin, i.e. αA-crystallin mutant R116C and αB-crystallin R120G (Spec. p. 9). The nature of the invention is such that many different proteins that are substantially similar to α-crystallin may or may not have biological activity. The state of the prior art is that even proteins that are 99% similar to the wild-type protein are at times not fully active. The relative

level of skill in this art is very high. The predictability as to what substantially similar protein will have which activity is zero.

When the factors are considered in their entirety, the Wands analysis dictates a finding of undue experimentation and thus, the claim is not enabled.

Applicants have currently amended claim 1 to recite active mutants thereof of αA- and αB-crystallin. Applicants point to page 9, line 30 to page 10, line 20 for support for active mutant forms of αA- and αB-crystallin. Applicants have also amended claims 14-16 to depend from claim 1. Applicants' arguments have been fully considered but they are not persuasive.

Firstly, there is no explicit definition for an "active mutant" of αA- and αB-crystallin. Applicants have provided only one specific example of a mutant αA- and αB-crystallin, i.e. αA-crystallin R116C and αB-crystallin R120G, on page 9 line 30 to page 10, line 20. However, Applicants have not specifically disclosed and/or define that αA- and αB-crystallin mutated at these residues are "active" mutants thereof; therefore, it is unclear what can be considered an "active" mutant of αA- and αB-crystallin. Further, it is known in the art that amino acid sequence identity of 50% does not guarantee structural similarity (Yuan et al. 1998 Proteins 30: 136-143), and that even a single point mutation in a polypeptide sequence can lead to surprising alterations in protein structure and activity (Sergel et al. 2000 J Virol. 74: 5101-5107). Therefore, given the unpredictability of the art, insertion, substitution, and/or deletion of amino acids into a wildtype protein, it is not clear if the molecular chaperone activity of any mutant αA- and αB- crystallin will be enhanced.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-11, 13-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 and its dependent claims are drawn to a method for enhancing molecular chaperone activity of α-crystallin, wherein step 1(c) recites observing an enhancement in chaperone activity of α-crystallin in the presence of Arg.HCl. It is unclear which protein (X) the enhancement in chaperone activity of α-crystallin is being observed with and/or compared against. The protein (X) needs to be explicitly recited in claim 1 since as currently written, there is an essential step missing from the claim. Further, claim 1 recites an active mutant thereof (of αA- and αB-crystallin). It is unclear what an active mutant is and/or what is considered to be an active mutant of αA- and αB-crystallin.

Claims 1(a), 1(b), 5-7 recite the limitation "α-crystallin" in the claim. There is insufficient antecedent basis for this limitation in the claim. The term should be replaced with "the α-crystallin."

Claims 5-8, 10-11, 16-18 recite percentages by which the chaperone activity of α-crystallin is enhanced or percentages at which the α-crystallin is protected (claims 10-11). It is unclear how these percentages were determined, i.e. by what method(s) were the enhanced chaperone activity and "protection" properties measured. The analysis method and conditions should be recited.

Claims 3-8, 10-11, 17-18 recite the limitation "Arg.HCl" in the claim. There is insufficient antecedent basis for this limitation in the claim. The term should be replaced with "the Arg.HCl."

Claim 7 recites aggregation systems. It is unclear what an aggregation system is or what is meant by an aggregation system.

Claims 15-16 recite a protective effect. It is unclear what is meant by "protective effect", i.e. protection against what?.

Claims 9, 13-14, 19-20 are included in this rejection because they are dependent on claim 1 and fail to cure the defect.

Claims 3-11, 13-20 are included in this rejection because they are dependent on claim 1 and fail to cure the defect.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marsha M. Tsay whose telephone number is 571-272-2938. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

July 18, 2007

M. Monshipouri

MARYAM MONSHIPOURI, PH.D.
PRIMARY EXAMINER